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DR. MELVIN W. GREEN

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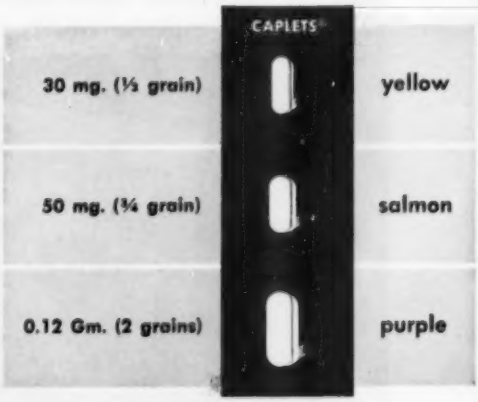

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AMERICAN JOURNAL OF PHARMACY

AND THE SCIENCES SUPPORTING PUBLIC HEALTH

Since 1825

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E D I T O R I A L

RECRUITMENT OF PHARMACY STUDENTS

IT takes no imagination whatsoever to appreciate the fact that how well pharmacy is practiced in coming decades will depend very largely, if not altogether, on the qualifications and motivation of the graduates in pharmacy which our colleges train. Whether we have pharmacy practiced on a high plane or a very low one then rests, in the final analysis, on the performance of our colleges of pharmacy. This fact is recognized by most educators, but what is not understood by many in the ranks of pharmacy is how far back in the scheme of things we must start in order to build soundly for the future.

Psychologists tell us what a person really is, what he aspires to be, and how well he may be expected to work toward attaining that goal is very largely determined and fixed by the time an individual finishes high school. Little, if any, change can be expected in the basic nature of the individual after this date. It is even likely that much of what a person is must be laid down in early childhood and is influenced primarily by the home environment and the training and guidance given by the parents. It is, therefore, an almost hopeless task to take young people into our colleges of pharmacy who are poor raw material, even more poorly motivated, and with no feeling whatsoever concerning the importance of serving one's fellow man and expect to graduate them after four, five, or even six years the kind of pharmacists the profession needs. College professors are only human and they do not possess magical powers. They may strive their utmost to change a self-centered, greedy individual into one who will put the welfare of his fellow-man above all other considerations but any success which they may feel they may have achieved is superficial indeed. It soon wears off once the student has escaped the surveillance of his teachers.

This, in essence, is exactly what is presently wrong with some pharmacists now in practice. They exploit the customer, feel that nothing is wrong with substitution, and are often dishonest in their dealings with others. It is not that they were not shown the proper way; neither can their teachers be blamed for not having so trained them that they keep strictly in the pathway of professionalism as they were urged.

There is a movement afoot today to make long-range plans to remedy much of this evil. In the coming years, it appears that very large numbers of young people will reach college age and the college population generally will be doubled in about 1965 over what it was in 1950. That there will be adequate numbers of young people seeking admission to pharmacy seems a certainty. The question is: *What kind of young people will they be?*

As it is presently constituted, pharmacy as seen by the public is practiced largely in a commercial atmosphere. It is small wonder then that those young people who see pharmacy only in its most superficial sense think of it only as a business and a very profitable one at that. It is this thought that makes many young people consider pharmacy as a career and they enter college with the intention of finishing as soon as possible so that they may engage in a business. Pharmacists, themselves, only too often add to the ranks of these poorly motivated, would-be pharmacists by directing to the colleges of pharmacy those boys and girls who have been outstandingly successful as salesmen, little realizing that this is perhaps one of the poorest qualifications that might be offered.

If a man or a woman is to practice pharmacy in the full sense of the word, he must of necessity enter the college of pharmacy with a spirit of dedication and a desire to render service in helping the sick and suffering. Whatever financial gain is expected must be a secondary consideration and not the primary reason for entering the field. The same thing could be said of each of the health professions; wherever one finds an outstanding practitioner of medicine, dentistry, nursing, or pharmacy, one finds just such a person. It would be a sad state of affairs indeed if all such professional people practiced with the profit motive as their only aim.

Colleges of pharmacy are beginning to appreciate the importance of getting dedicated young people interested in a career in pharmacy. A Committee on Recruitment Aids of the American Association of Colleges of Pharmacy has embarked on a very extensive program for motivating and recruiting just such young people for pharmacy. At some date, far distant in the future, a pharmaceutical historian may well point to this program as one of the most significant undertakings of American pharmacy in the twentieth century. Its full results will not be realized in our lifetime but they may well bring about changes in our profession which today would be unbelievable.

L. F. Tice

PHARMACEUTICAL EDUCATION AND THE WISCONSIN IDEA *

By Melvin W. Green **

THIS is a joyous occasion. The Greens are happy for today is for them a homecoming and a high honor. The staff and students of the School of Pharmacy are rejoicing for they have at hand tools for developing a stronger program in pharmaceutical education. Pharmacists of the state are joyous for they see, once again, Wisconsin pharmacy demonstrating the leadership that has been theirs for many decades. Yes, the time of dedication of new quarters for the School of Pharmacy is a time for rejoicing; it is also a solemn occasion of rededication to an ideal for all of us.

Pharmaceutical education in the United States can be thought of, historically, in terms of several rather distinct eras. Initially all such training was on a preceptorship basis and, indeed, until 1821 there were no centers of formal instruction. The first school of pharmacy was established in Philadelphia almost concurrently with the publication of the first United States Pharmacopoeia. Other schools were soon established, largely in the East. These schools were started by the profession itself and were often more proprietary than public in character. It was not until some 70 years later that the University of Wisconsin started offering instruction in pharmacy. From its inception, the School of Pharmacy at Wisconsin has been destined to be a "first" in the phases of pharmaceutical education of moment. It was first to offer pharmacy on a 4-year baccalaureate basis. Under the scholarly leadership of Professor Kremers, it was the first to offer the Ph. D. in a pharmaceutical science. It was the first to pay obeisance to the importance and the glory of pharmacy's past by establishing a chair in the history of pharmacy. If my data are correct there are 13 Deans in our 74 Colleges of Pharmacy who were educated at the graduate level in Wisconsin and at least 5 other Deans who obtained Ph. D.'s under Wisconsin trained men. This is cited as evidence that the borders of the campus are the borders of the nation.

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* An address presented at the dedication of the new building of the School of Pharmacy, University of Wisconsin, Oct. 22, 1955.

** Director of Educational Relations, The American Council on Pharmaceutical Education.

There are many persons within this room far more able than I to reconstruct Wisconsin's past. I hope that you will forgive me if I dismiss it with the statement that without this past, American Pharmacy's poverty would be so abysmal, her problems would have been so much more acute, that, one wonders if she could have survived the vicissitudes of the present. Rather than dwell upon the past, I hope that you will bear with me while I discuss some problems of the present and the future, in relation to the Wisconsin Ideas, as I see them.

Some time ago I had occasion to review the philosophy of education with a group of hospital pharmacists meeting at the University of Chicago. In mulling over what to say upon that occasion, I was struck by the headlines of the front page of the newspaper in Chicago that evening. Let me read these captions to you: "Report Ford Proposes Plan for Job Security"; "India Priest Slashed to Death Here"; "University of Chicago Opens Drive to Raise $32,779,000"; "Punish 28 Co-Eds for Night Out"; "Occasional Showers Late Tonight or Friday"; "Refuses to Drop 'Slur' on 'Test Tube' Babies"; "Woman Flies Jet at Record Pace"; "Offer State Minimum Wage Bill"; "Time Short to Find Nag that Bit Girl"; "Race Results"; "83 Hurt in Subway Crash"; "Ike Tees Off". . . . Now this is the stuff that makes up the here and now. This is the news that everyone from the corner bootblack to the President of the Bank tries to interpret. It touches upon nearly every facet of American life—the health sciences, public affairs, morals, meterology, aviation, economics, the fine arts, higher education, journalism, international affairs, woman's place in society, geography, history—there it is distilled into a few pennies worth of wood pulp and printer's ink. The interpretation of these news stories must often lead the citizen beyond thought to action. I suppose every person who can read, has his reaction to these news items. The point is that the community looks to and has a right to look to the college graduate for informed leadership in a multitude of affairs.

This brings us to one of the broad problems facing all of the professions: how to get the professional man into the main streams of community life not just as a skilled professional man, but as a whole man. Let me quote from Professor Baker Brownell on the relation of the whole man to the community. "The community, to put it very briefly, is a group living under conditions in which people can know each other well. This knowing each other well includes, I think,

frequent face-to-face relationships. It includes diversified relationships as to age, sex, skill, function, and mutual service to each other. It includes direct cooperative relationships in many of the main activities of life and some sense of 'belonging' or solidarity. It involves above all a rather small group in which people may know each other as whole persons rather than as functional fragments. I shall not elaborate on this description of the human community except to suggest that this integral relationship of men as whole human beings with each other is the source and sanction of our values and the basis for whatever seems of worth in the process of living. Human values, in other words, are centered and sanctioned in the human community."

How can we get the pharmacist to take his proper place in the community as a whole man? It seems to me that one obvious and important answer to this, is to broaden his educational base until we have brought about a true enlargement of mind so that all things, pharmaceutical and otherwise, are referred severally to their true place in the universal system, their respective values are comprehended and their mutual dependence understood. This broadening effect should be one of the prime goals for the extended program of pharmaceutical education now on the drawing boards. Surely the pharmacist should not be denied the education that something like 20 per cent of his patrons in the near future will have. Wisconsin has been a leader over the years in her insistence upon education for life as opposed to education for a living. Surely the future will not detract from this important philosophy of education which is a part of the Wisconsin Idea. I like to believe that Wisconsin will continue to "serve its time without yielding to it".

Those of you who are active at prescription counters know that about 75 per cent of the prescriptions today could not have been dispensed or compounded a decade ago. That is a measure of the speed with which new drugs become available. If such a rate is to be maintained, and all evidence points in that direction, how can education keep pace? Obviously within 5 years after graduation, much the pharmacist has learned has become obsolete and he is confronted with a whole new world of facts. It seems to me that the only sound solution is thorough education in the fundamental sciences ancillary to pharmacy. The student must be given an opportunity to know the basic ideas, theories and concepts, not just the facts, in the various branches of chemistry, physiology, bacteriology and other sciences in order that he can read the professional literature of the future with

reasonable intelligence. When Wisconsin first made pharmacy available on a 4-year basis in 1892, the principal objectives were to broaden the base of the pharmacist's education and to provide a better background in the basic sciences.

It is the professional side of the curriculum that naturally interests us most as pharmacists. Time will not permit the discussion of all of the problems that exist in this area or that one can anticipate in the future. There are a few that I would like to touch upon, however.

As you well know, the education of a pharmacist has always been biphasic. Part of his education has been obtained in our colleges and that formal education has been supplemented, traditionally, by training on the job or internship. In this fast-moving pharmaceutical world those responsible for both phases of the educational process are searching for more efficient and effective ways of accomplishing their ends. This means that faculties and State Boards need to do more frequently what has been done in this state from time to time, that is, sit down together occasionally and separate that which is best learned on the job from that best learned in the colleges. To teach a young man or young lady in college to wrap a package, to take an inventory and many other such things is not educationally sound any more than for a store owner to attempt to teach these young people organic chemistry. While it is clear that the responsibility for proper practical experience lies with the State Board (and ultimately with the individual store owners and managers) and that for collegiate education lies with the faculties, this does not mean that these phases are mutually exclusive. There is a growing realization that each group has a need for understanding developments in the other area. If the members of the profession have a clearer understanding of the goals of formal education, they should be more helpful and more concrete in their internship programs. For faculties to fail to build their more formal programs, at least in part, with a full knowledge of the practical experience objectives and attainments is to diminish the effectiveness of the overall professional education program. Wisconsin has had a long tradition of effective working relations between the educators, the licensing boards and the profession at large. American pharmacy is going to continue to look to Wisconsin for ideas and ideals in these interrelationships.

The character of pharmacy practice is changing. The community pharmacist no longer compounds and manufactures to the same extent

that he once did. Currently only 7 to 15 per cent of physician's prescriptions are actually compounded. There are those who read into this fact the idea that compounding and formulation should be deemphasized. Personally I am inclined to interpret the situation otherwise. New and more versatile pharmaceutical adjuncts are available as are better techniques for combining them with drugs. Pharmacy is replacing the descriptive approach by leaning heavier upon the physical-chemical approach. Here is the area where the pharmacist can render an important service to physicians and other members of the health team. To argue that compounding is not important because as a statistic it is represented by a low number is like saying atropine is not an important drug because it is administered in doses of only a fraction of a milligram.

New drugs become available at almost a terrifying rate. The busy physician finds it difficult to keep pace and welcomes a source of unbiased, but reliable information. To meet this need there is a growing emphasis on pharmacology and the biological sciences to assist the pharmacist in talking the language of medicine and the other health sciences and in counseling more effectively. Currently only two Schools of Pharmacy in the United States do not offer laboratory instruction in pharmacology. The pharmacist cannot neglect this phase of his education, if he is to be the authority on drugs.

One of the significant pharmaceutical sparks that splintered off from the Wisconsin Idea was the establishment in 1913 of a kind of pharmaceutical extension service under the guise of a Pharmaceutical Experiment Station. While this institution was a casualty of the depression of the thirties, the concept did not die. There are now some two or three significant extension divisions attached to colleges of pharmacy and others at least at the wishing stage. During this era when the practicing profession has a varying educational background, when progress and changes in the field are so rapid, when economic and legal pressures are so great, a consultative extension service would appear to be of great value. One such service which it has been my good fortune to observe in its infancy is providing a translation service on foreign prescriptions in an area where such prescriptions are numerous, answers several telephone inquiries daily, has provided professional research on technological as well as economic problems, has set up seminars for pharmacists, and for junior executives in the pharmaceutical industry, keeps pharmacists widely informed by monthly newsletters, takes an important position in a center for

toxicological information on household items of potential concern, and provides several other services. The need for such services appears to be so great that the Director indicated that the time is approaching rapidly when they will have to define the kinds of service that they will not render in order to prevent dilution. Surely here is the Wisconsin Idea at work in a most practical way.

The hospital is growing in importance in the American health program. In 1954 the nation's 6,970 hospitals cared for over 20 million patients. At present only slightly more than half of these hospitals have a pharmacy in the accepted sense of the word but there are now 4,157 full-time and 786 part-time pharmacists servicing these institutions. Educationally there is as much need for separating formal education from on-the-job training in preparing a hospital pharmacist as there is in educating a pharmacist for community practice, but there is a need, also, for academic programs that will prepare pharmacists for better institutional practice. The growing trend for erection of relatively small hospitals in more rural communities means that community pharmacists will often have to provide the professional pharmaceutical service for these smaller units on a part-time basis. The colleges can provide a distinct service in assisting such pharmacists by providing in-service seminars and extension services to acquaint them with the problems of institutional care.

Pharmacists are becoming increasingly aware of the fact that they are often the sole professional intermediary in the distribution of substances used for self-medication. This carries with it an increasing responsibility to place the ringing of the cash register secondary to the patron's welfare. We are beginning to recognize, also, the implications of the fact that the pharmacist sees every day more persons when they are well than any other members of the health team. In an era of preventative medicine we must be more alert to our central position in community health than we have been in the past. Is it not strange that on most campuses the only courses offered in health education are for school teachers?

In the recent PHARMACEUTICAL SURVEY so well generalled by President Emeritus of Purdue University, Edward C. Elliott, it is written: "After all has been said and done, it may be concluded that the outstanding factor determining the future of the profession of pharmacy is fundamentally moral in nature. The profession must contain a far greater proportion of members who are very sharply jealous of the high reputation of the profession and who, by energetic

cooperation, are determined to protect that reputation." While matters of such broad moral concern spring out of the philosophy of a broad university education, they cannot be left to chance. Neither can they be made a matter of indoctrination. I believe the pharmacy student can be taught to think in ethical terms. By patient discussion the student can be shown the long view relating to the consequence of his acts. I know of no phase of his education that is more practical in its ultimate effect on the profession than the degree of obedience to the unenforceable that we can attain.

I now come to an area which at Wisconsin has always been of the utmost importance—scholarship and research. Research is interested in discovering new facts and ideas; scholarship takes the direction of correlating, interpreting, extending and illuminating principles and facts rather than discovering new ones. Vital teaching is integrating scholarship and research with communication so as to stimulate self-education on the part of the student. As Professor Crowley of Stanford University expresses it "without research, scholarship degenerates into fatuous verbalism; without scholarship, research decays into a mere collection of elaborate trivia; without scholarship and research, teaching becomes a bromidic prattling."

If pharmaceutical teaching is to be lifted from the vocational education class, we will need more teachers educated at the graduate level to understand the needs for the scholarly and research approach. We now have nearly 500 Ph. D.'s teaching pharmaceutical subjects in our 74 colleges. We have increased the total number of graduate students during the past decade from around 85 to about 600. Great store should be placed on these numbers, but the goal must be shifted from the quantitative to the qualitative. The historical fact that pharmacy was the mother of several of our present-day sciences has little meaning if she does not continue to hold high standards in scientific research. American pharmacy is going to continue to look to Wisconsin to strengthen the quality of pharmaceutical research and to provide dedicated and capable teachers.

Industrial pharmacy has shifted its emphasis from the emperical to the scientific approach. Whether pharmacy has maintained its scientific position in this change is open to question. In terms of percentage of sales, probably no industry plows back more funds into research. It is a research-minded industry. Relatively large numbers of pharmacists are employed by the industry in every capacity including research. It cannot be said that the pharmaceutically

trained have, in general, reached the central position that we think they deserve. The fault lies in part with blind spots in the industry, but a large part of the blame we in the Colleges must assume. The need for men with the kind of training obtained at Wisconsin now seems to be almost infinite so far as the industry is concerned. I am not entirely convinced, however, that the best way to meet this need is to channel more persons with graduate degrees into industry. Perhaps in the long view more effective research workers will be produced by encouraging the more able graduates to take teaching positions in colleges of pharmacy having graduate programs.

But, Ladies and Gentlemen, you are not here to listen to the questionable wisdom of one individual but rather to dedicate the new edifice of the School of Pharmacy. We are here to set aside this edifice for the procreation of the profession and the extension of professional knowledge. But a building is an inanimate thing of brick and mortar and steel—alone it can do none of these things. Perhaps it is ourselves that we should dedicate.

Dean Uhl, at this important moment, those of us who are teachers are stating our determination to prepare the young to meet adequately the problems they encounter as they approach to maturity by strengthening our scholarship, vitalizing our research and improving our communication. We recognize that a good teacher works hard to get students to work hard for themselves. Always our objective is the student's curiosity, his imagination, his thought, his insight, his judgment—not ours. We recognize that there is no greater calling than ours and that the responsibility is great, but we desire to live up to the opportunities that these new quarters bring us.

Dean Uhl, those of us who are members of the Board of Pharmacy rededicate ourselves to the responsibilities to protect the public and the profession from those forces that would destroy the profession by destroying public confidence. We are mindful that ours is the task to guard the gateway to the profession and to protect and promote continuously those vital professional interests compatible with the welfare of the public.

Dean Uhl, those of us who are still students wish to dedicate ourselves to the profession as well. We are mindful that we will be carrying the torch onward soon. We want to learn from every source we can so that we will be prepared to be the leaders in the community and the profession one of these bright tomorrows. We are mindful that our fingers are all thumbs, that we rush too often

into places where even the angels fear to tread. But be patient with us, challenge our capabilities, cherish us and we will not let you down.

Dean Uhl, there are those of us who practice the profession in our communities, in hospitals, in the industry and various distributive links. We, too, are happy for you that these fine new tools are available. We recognize that we have arrived at another milestone for pharmacy and we ask to be a part of it. We hope that you consider us as members of your staff W. O. C., which is army language for "without compensation", for we are pledging ourselves to accept your graduates, not as finished pharmacists, but as persons beginning to practice pharmacy. We will do all we can to give them the benefit of our experience patiently. At the same time we are reminding ourselves that we are the profession, that our responsibility is great, that what we are speaks louder than what we say. In the paraphrased words of the Code of Ethics of the American Pharmaceutical Association we recognize anew that the practice of pharmacy requires knowledge, skill and integrity; therefore the State laws restrict the practice of pharmacy to persons with special training and qualifications, and license to us privileges which are denied to others. Accordingly we recognize our responsibility to the State and to the community for their well-being and we fulfill our professional obligations honorably.

We all so rededicate ourselves on this important occasion.

IN VIVO EXPERIMENTS WITH CARCINOGENS. VIII

By John R. Sampey, Professor of Chemistry, Furman University, Greenville, S. C.

THE extent of the interest in agents inducing cancer in animals and man is reflected in the 1250 articles surveyed by the author in this and previous studies (156, 157). The present study shows continued interest in methylcholanthrene, benzanthracenes, radioisotopes, aromatic amines, estrogens, diet, smoking, and industrial carcinogens as topics receiving special attention today.

I. Inorganic Chemicals

Radioisotopes. Radiothyroidectomy caused pituitary tumors in mice (38, 41, 60). Single injections of Sr^{89} induced bone sarcomas in mice (49). Therapeutic doses of P^{32} resulted in oseogenic tumors in 3 of 385 mice (127). Studies have been made on neoplasms in survivors of atomic bombings (128, 172). Attention has been called to the dangers from radioactivity in the therapeutic use of thorotrast (85, 198).

Beryllium. Injections of beryllium compounds in rabbits produced bone sarcomas (83, 171).

II. Hydrocarbons

Methylcholanthrene. MC continues to be the most used hydrocarbon to induce a broad spectrum of neoplastic growths in experimental animals (6, 10, 20, 91, 92, 117, 121, 122, 123, 143, 164, 174, 177).

Benzanthracenes. Repeated applications of dimethylbenzanthracene, DMBA, produced skin cancer (93, 167). This hydrocarbon induced ovarian tumors in 53 of 88 virgin mice (75), and wounds in rabbits treated with DMBA developed neoplasms much sooner (25). DMBA and 1-isopropyl-5-methylazulen caused carcinoma in mice (9). Dibenzanthracene produced lung tumors in mice (68, 69). Several methylbenzanthracenes (37, 104), and halogen-benzanthracenes (104) caused neoplasms in rodents.

Benzpyrene. Investigations have been made on the formation of skin cancers from benzpyrene (48, 51, 135, 160). Agate and associates (2) demonstrated that the hypophysis was not essential to the formation of benzpyrene neoplasms, and Von Haam and Searpelli (190) caused carcinoma of the cervix and vagina by painting mice with this hydrocarbon.

Tars. Tar ointment has produced human epithelomas (3, 4, 19). Malignant papillomas were induced in mice by coal tar distillates (142).

Atmospheric Hydrocarbons. The carcinogenic action of hydrocarbons in urban centers has been investigated (30, 31, 95, 96, 97).

III. Organic Nitrogen Compounds

Acetylaminofluorene. AAF induced neoplasms of the liver (116 125), auditory sebaceous gland (101), papillomatosis of the bladder (179), and with croton oil or DMBA it caused skin tumors (150). Substituted AAF derivatives induced breast tumors and squamous cell carcinoma of the forestomach of mice (125).

Azo Compounds. Hepatomas have been caused by p-dimethylaminoazobenzene, DAB (138), 2′,4′,6′-trifluoro-DAB (124), 3′-methyl-DAB (149), and p-dimethylaminobenzene-1-azo-2-naphthalene (131). 3′-methyl-DAB plus ACTH induced bile duct carcinoma in hypophysectomized rats (148).

Aromatic Amines. Amino-tumors of the bladder have been reported in workers handling alpha- and beta-naphthylamine, benzidine, and other aromatic amines (14), and Vaggi (189) described malignant vesical lesions in 16 workers exposed similarly. Hyperplastic nodules followed feeding young rats 4-acetylaminobiphenyl (188), but this amine produced no neoplasms by intramuscular injections (153). Methyl derivates of 4-aminodiphenyl produced intestinal and bladder tumors in rats (192).

Thioacetamide and Sulfonamides. Thioacetamide induced cirrhosis of the liver (5, 145), and cancer of the bile duct (59). Several sulfonamides caused renal adenocarcinomas and sarcomas in rodents (16).

Thiouracil. This chemical induced cell proliferations in the thyroid gland of hamsters (99), and it increased the incidence of lymphogenous leukemia in mice (55).

Urethane and Methylformamide. Lung tumors were induced in mice by urethane (26, 81), and this chemical caused skin tumors (151). Urethane and methylformamide before or after inoculation with leukemia caused hepatic virus disease to become active in mice, but neither drug had any effect on the neoplasms (24).

Alloxan. Alloxan produced liver necrosis, and given with chloroform the effect was increased (110).

Ethyleneimines. Several of these organic nitrogen compounds were carcinogenic in rodents (191).

Nitrogen Mustard. Radiothyroidectomy followed by injection of nitrogen mustard induced pituitary tumors in mice (41).

Dibenzcarbazole and Benzacridines. Dibenzcarbazole injections caused carcinoma in the bladder of a dog (21). Several benzacridines were found fairly carcinogenic to the skin of mice (28), while others failed to produced neoplasms in the skin of rats (152).

IV. Hormones

Estrogens and Androgens. Estrogens induced breast cancer in mice (129, 146) and pituitary adenomas in mice (53). They also increased the incidence of visceral lymphomatosis in chickens (36), and potentated the X-ray induction of lymphomas in mice (183). Diethylstilbestrol, stilbestrol and estradiol pellets all caused epithelial cancers (52). The estrogen, ovacyline, produced adenocarcinoma in a patient (197). Estradiol in combination with progesterone acted as a promoting agent for MC tumors (87). Pituitary tumors were produced in rats by estradiol and diethylstilbestrol (47). The latter hormone also caused renal tumors in hamsters (73, 74), adenomas of the pituitary in rats (109), and breast cancer in mice (147). This estrogen also increased the growth of transplanted mammary fibroadenoma in male rats. Sarcoma S-180 grew faster in hydro-uteri than in the intact uterus (72). Muhlbock (130) studied the genesis of ovarian tumors in mice in parabiotic union.

Testosterone increased the lethal effects of X-rays in mice (42), and it increased the incidence of lymphomatosis in chickens (36).

Castration. Castrated mice developed adrenal and pituitary neoplasms (41, 111, 154, 168).

ACTH and Cortisone. ACTH increased malignant lymphoid tumors in mice (169, 170). Both ACTH and cortisone promoted

the transplantation of human neoplasms in animals (65, 70). With 3′-methyl-DAB ACTH caused bile duct carcinomas in rats (148). Cortisone increased the production of MC sarcoma grafts in mice (27).

Pituitary and Thyrotropin. Pituitary hormone caused breast cancer in mice (129), and it promoted the growth of human neoplasms in rats and hamsters (184). Sarcoma grew faster in hypophysectomized rats (106). Thyrotropin promoted the incidence and growth of lymphomas in gonadectomized, irradiated mice, but growth hormone had but little effect (133). Pituitary and thyrotropin were less effective than ACTH in causing 3′methyl-DAB neoplasms in rats (148).

Thyroid and Thiouracil. The former increased and the latter reduced the mortality of mice exposed to X-rays (17).

Follicular Hormone. Lengthy treatment of a patient with this hormone was reported as inducing an adenoma of the hypophysis (115), and the hormone hastened the growth of sarcoma grafts in dogs (181).

V. Miscellaneous Agents

Occupational. Occupational hazards from carcinogens has received a number of investigations (1, 14, 67, 76, 77, 78, 79, 80, 98, 108, 139, 186, 187, 189).

Smoking. The search for carcinogens in tobacco attracted a number of investigators (32, 33, 34, 45, 61, 62, 63, 64, 94, 105, 132, 144, 165, 194, 195, 196).

Neoplastic Tissues and Extracts. Cell free extracts from leukemic tissues produced neoplasms in the parotid gland and adrenal gland of mice (57, 178). Differences in susceptibility to leukemia have been noted in mice (58, 71). Frozen tumor grafts grew faster in rabbits (29). Grafts grew faster in mice pretreated with filtrates of enzyme digested tumors (88). Pretreatments with lympholized tissue or extracts of neoplasms hastened tumor growth (117, 118, 126, 141, 182). Cell suspensions of various neoplasms have been tested (35, 54, 90). Injections from fast growing breast tumors or large tumors showed increased effects on tumor growths (112, 113). The effects from first and second generation transplants of breast tumors have also

been studied (163). Transplantation of human tumors into animals has been further investigated (102, 107, 134).

Normal Tissues and Extracts. Crude beef anterior suspensions enhanced the growth of fibroadenoma but not fibrosarcoma in rats (119, 120). Normal tissue inocula caused breast adenocarcinoma in mice to grow faster (161). Whole blood injections enhanced the growth of Sarcoma I in mice (173). Cell suspensions of the skin of one-day old rats caused malignant tumors (180). Tumor homografts grew only in mice pretreated with antiserums (89).

Diet. Low choline diet produced cirrhosis of the liver in rats and dogs (43, 44, 159). Ethionine caused carcinoma in rat livers (46), and a high pyridoxine diet resulted in more AAF liver tumors in rats (66). Acetamidofluorene fed rats with tryptophane and casein hydrolysate caused carcinoma of the bladder, while beta-naphthylamine in the same diet resulted in liver tumors (23). A methionine-deficient diet increased azo dye carcinogenesis in rats (185). A synthetic diet containing pantothenic acid stimulated the growth of Walker S-256 (166). Low iodine diet produced thyroid tumors in rats (8), and a low protein diet increased the susceptibility of rats to X-rays (84). Cancer of the liver has been related to the diet of natives of the Gold Coast (11).

Tumor Agent. The mammary tumor inducing factor has continued to attract investigators (15, 39, 56, 100, 103, 114).

Polymers. Implants of a number of commercial plastics and polymers induced fibrosarcoma in rodents (12, 136, 137).

CCl_4. Small doses of CCl_4 over long periods induced fibrosis of the liver (7).

Phenols. A number of phenols produced carcinomas in mice (22).

Adenosine. Four derivatives stimulated Rous sarcoma (82).

Senecio Alkaloids. The relation of these alkaloids to the induction of neoplasms in animals and man has been studied (158, 162).

Enzymes. Hyaluronidase increased the growth of chicken sarcoma (50).

Synkavit. This agent increased radiation sickness in rats (86).

Plant Hormones. These agents induced tumors on unfertilized ova of rats (140).

Chloramphenicol. Lymphatic leukemia in mice was enhanced by this agent (175).

Folic Acid Antagonists. Weston and Guin (193) warn of epithelial atypias in children given this therapy.

Injury. Hyperplasia of the ear was produced in rabbits by mild injury with metal tags (118). Thermal injury induced skin tumors (155).

Emotional Stress. The effect of long-standing emotional stress on the incidence of human cancer has been investigated (18, 176).

Croton Oil. No skin neoplasms were produced in mice by Xrays and croton oil (13).

Allergy. No relation has been established between Hodgkin's disease and allergy of patients (40).

Dibenzcarbazole. This chemical induced a carcinoma of the bladder in a dog (21).

Acknowledgments

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REFERENCES

(1) Abeshouse, B. S., *Urol. and Cutan. Rev. 55,* 65-78 (1951).

(2) Agate, F. J. Jr., *Cancer Res. 15,* 6-8 (1955).

(3) Alexander, J. O. and Macrosson, K. I., *Brit. Med. J.* 1089 (1954).

(4) Alexander, J. O. and Macrosson, K. I., *ibid.* 287 (1955).

(5) Ambrose, A. M., *et al., J. Ind. Hyg. Tox. 31,* 158-61 (1949).

(6) Andervont, H. B. and Dunn, T. B., *J. Natl. Cancer Inst. 14,* 329-40 (1953).

(7) Aterman, K., *Arch. Path. 57,* 1-11 (1954).

(8) Axelrad, A. A. and Leblond, C. P., *Cancer 8,* 339-67 (1955).

(9) Barton, H., *Arch. Exptl. Path. 223,* 443-9 (1954).

(10) Bartra, B. K., *Nature 175,* 388 (1955).

(11) Bergouniou, J. L., *et al., Sem. Hop. Paris 29,* 324-34 (1953).

(12) Bering, E. A., *et al., Cancer Res. 15,* 300-1 (1955).

(13) Biagini, C., *et al., Tumori 40,* 454-67 (1954).

(14) Billiard-Duchesne, J. L., *Presse Med. 57,* 615-6 (1949).

(15) Bittner, J. J. and Frantz, M. J., *Proc. Soc. Exptl. Biol. Med. 86,* 698-701 (1954).

(16) Bjerre-Hansen, P. and Bichel, J., *Acta Radiol. 37,* 258-65 (1952).

(17) Blount, H. C. Jr. and Smith, W. W., *Science 109,* 83-4 (1949).

(18) Blumberg, E. M., *et al., Psychosom. Med. 16,* 277-86 (1954).

(19) Bond, W. H., *Brit. Med. J.* 1226 (1954).

(20) Bonser, G. M., *J. Path. Bact. 68,* 531-46 (1954).

(21) Bonser, G. M., *et al., ibid. 68,* 561-4 (1954).

(22) Boutwell, R. K., *et al., Proc. A. A. Cancer Res. 2,* 6-7 (1955).

(23) Boyland, E., *et al., Brit. J. Cancer 8,* 647-54 (1954).

(24) Braunsteiner, H. and Friend, C., *J Exptl. Med. 100,* 665-74 (1954).

(25) Breedis, C., Proc. A. A., *Cancer Res. 2,* 7 (1955).

(26) Burdette, W. J., *ibid. 2,* 8 (1955).

(27) Bussolati, D. C., *Tumori 40,* 571-9 (1954).

(28) Buu-Hoi, M., *J. Chem. Soc.* 4867-9 (1952).

(29) Casey, A. E., *et al., Proc. Soc. Exptl. Biol. Med. 77,* 221-4 (1951).

(30) Clemo, G. R., *Chem. and Ind.,* 957-64 (1953).

(31) Clemo, G. R. and Miller, E. W., *ibid.* 38 (1955).

(32) Cooper, R. L. and Lindsey, A. J., *ibid.* 1260-1 (1954).

(33) Cooper, R. L., *et al., ibid.* 1418 (1954).

(34) Cutler, S. J. and Loveland, D. B., *J. Natl. Cancer Inst. 15,* 201-11 (1954).

(35) Davis, O. S. and Doyle, L. P., *Am. J. Vet. Res. 10,* 85-91 (1949).

(36) Davis, O. S., *et al., ibid. 11,* 428-36 (1950).

(37) DeClerca, M., *et al., Compt. Rend. 148,* 812-4 (1954).

(38) Dent, J. N., *et al., Cancer Res. 15,* 70-5 (1955).

(39) Dmoskowski, L., *et al., Proc. A. A. Cancer Res. 2,* 13 (1955).

(40) Dworin, M., *et al., Cancer 8,* 128-31 (1955).

(41) Edelmann, A. and Gorbman, A., *Proc. A. A. Cancer Res. 2,* 13-4 (1955).

(42) Ellinger, F., *Proc. Soc. Exptl. Biol. Med. 74,* 616-9 (1950).

(43) Engel, R. W. and Alexander, H. D., *Fed. Proc. 10,* 382 (1951).

(44) Erickson, C. C. and Goebbell, W., *ibid. 8,* 354 (1949).

(45) Essenberg, J. M., *et al., Proc. A. A. Cancer Res. 2,* 14-5 (1955).

(46) Farber, E., *ibid. 2,* 15 (1955).

(47) Fels, E., *Compt. Rend. 144,* 1226 (1950).

(48) Fiala, S., *et al., Proc. A. A. Cancer Res. 2,* 15 (1955).

(49) Finkel, M. P., *et al., ibid. 2,* 16 (1955).

(50) Fujita, K. and Iwase, S., Nogoya *J. Med. Sci. 16,* 298-305 (1953).

(51) Gagne, F., *et al., Bull. Assoc. Franc Cancer 4,* 270-9 (1954).

(52) Gardner, W. U., *Proc. A. A. Cancer Res. 2,* 18-9 (1955).

(53) Gardner, W. U., *J. Natl. Cancer Inst. 15,* 693-709 (1954).

(54) Goldie, H., *et al., Cancer Res. 15,* 263-7 (1955).

(55) Grad. B., *et al., Proc. A. A. Cancer Res. 2,* 20 (1955).

(56) Graff, S., *et al., Cancer 2,* 755-62 (1949).

(57) Gross, L., *Proc. A. A. Cancer Res. 2,* 21 (1955).

(58) Gross, L., *Proc. Soc. Exptl. Biol. Med. 88,* 64-6 (1955).

(59) Gupta, D. N., *Nature 175,* 257 (1955).

(60) Helmi, N. S. and Gude, W. D., *Am. J. Path. 30,* 403-19 (1954).

(61) Hammond, E. C., *Conn. Med. J. 18,* 3-9 (1954).

(62) Hammond, E. C., *Cancer 7,* 1100-8 (1954).

(63) Hammond, E. C. and Horn, D., *J. A. M. A. 155,* 1316-28 (1954).

(64) Hammond, E. C., *J. Am. Pharm. Assoc. Prac. Pharm. Ed. 15,* 537-41 (1954).

(65) Handler, A. H., *Proc. A. A. Cancer Res. 2,* 22 (1955).

(66) Harris, P. N., *ibid. 2,* 22 (1955).

(67) Heller, J. R. Jr., *Arch. Ind. Hyg. 2,* 390-9 (1950).

(68) Heston, W. E., *J. Natl. Cancer Inst. 10,* 119-24 (1949).

(69) Heston, W. E. and Dunn, T. B., *ibid. 11,* 1057-72 (1951).

(70) Hoch-Ligeti, C. and Hsu, Y. T., *Science 117,* 360-1 (1953).

(71) Hoecker, G., *et al., Cancer Res. 15,* 9-14 (1955).

(72) Homburger, F., *et al., Proc. A. A. Cancer Res. 2,* 25 (1955).

(73) Horning, E. S. and Whittick, J. W., *Brit. J. Cancer 8,* 451-7 (1954).

(74) Horning, E. S., *ibid. 8,* 627-34 (1954).

(75) Howell, J. S., *et al., ibid. 8,* 635-46 (1954).

(76) Hueper, W. C., *Public Health Repts. Suppl. 209,* 1-69 (1949).

(77) Hueper, W. C., *South. Med. J. 43,* 118-24 (1950).

(78) Hueper, W. C., *Acta Unio Intern. Contra Cancr. 6,* 1295-1324 (1950).

(79) Hueper, W. C., *Arch. Path. 58,* 475-523 (1954).

(80) Hueper, W. C., *ibid. 58,* 645-82 (1954).

(81) Imagawa, D. T., *et al., Proc. A. A. Cancer Res. 2,* 26 (1955).

(82) Jakubovic, A., *et al., Chem. Listy 48,* 1875-7 (1954).

(83) Janes, J. M., *et al., J. Bone and Joint Surg. 36B,* 543-52 (1954).

(84) Jennings, F. L., *Proc. Soc. Exptl. Biol. Med. 72,* 187-91 (1949).

(85) Jentzer, A., *J. Inter. Coll. Surg. 23,* No. 1, 12-5 (1955).

(86) Jolles, B. and Laws, J. O., *Brit. J. Cancer 8,* 513-21 (1954).

(87) Jull, J. W., *J. Path. Bact. 68,* 547-59 (1954).

(88) Kaliss, N. and Day, E. D., *Proc. Soc. Exptl. Biol. Med. 87,* 208-11 (1954).

(89) Kaliss, N., *et al., Proc. A. A. Cancer Res. 2,* 27 (1955).

(90) Karnofsky, D. A., *Ann. N. Y. Acad. Sci. 55,* 313-29 (1952).

(91) Kirschbaum, A. and Liebelt, A. G., *Proc. A. A. Cancer Res. 2,* 28-9 (1955).

(92) Klein, M., *J. Natl. Cancer Inst. 14,* 1137-45 (1954).

(93) Klein, M., *Proc. A. A. Cancer Res. 2,* 29 (1955).

(94) Korteweg, R., *Brit. J. Cancer 8,* 34-9 (1954).

(95) Kotin, P., *et al., Arch. Ind. Health 11,* 113-20 (1955).

(96) Kotin, P. and Falk, H. L., *Proc. A. A. Cancer Res. 2,* 30 (1955).

(97) Kotin, P. and Hueper, W. C., *Pub. Health Rep. 70,* 331-3 (1955).

(98) Kreyberg, L., *Brit. J. Cancer 8,* 605-12 (1954).

(99) Kroon, D. B., *Acta Endocrinol. 8,* 343-61 (1951).

(100) Law, L. W., *Ann. N. Y. Acad. Sci. 57,* 575-83 (1954).

(101) Laws, J. O., *et al., Cancer Res. 15,* 139-42 (1955).

(102) Lemon, H. M., *et al., Science 115,* 461-5 (1952).

(103) Liebelt, A. G. and Kirschbaum, A., *Proc. A. A. Cancer Res. 2,* 31-2 (1955).

(104) Lindner, A. and Muller, A., *Scientia Pharm. 22,* 224-8 (1954).

(105) Lindsey, A. J., *Brit. Med. J.* 1352 (1954).

(106) Loeffer, J. B., *Cancer 5,* 161-2 (1952).

(107) Lumb, G., *Brit. J. Cancer 8,* 434-44 (1954).

(108) Macdonald, I., *J. A. M. A. 157,* 5-7 (1955).

(109) Maisin, J. and Meersseman, F., *Compt. Rend. 144,* 442-4 (1950).

(110) Martin, J. M., *Rev. Soc. Argentina Biol. 29,* 103-7 (1953).

(111) Martinez, C. and Bittner, *J. J., Proc. A. A. Cancer Res. 2,* 33 (1955).

(112) Martinez, C., *et al., Cancer Res. 15,* 442-4 (1955).

(113) Martinez, C., *et al., ibid. 15,* 469-72 (1955).

(114) Martynova, R. P. and Shabad, L. M., *Arkh. Patol. 11,* No. 3, 36-9 (1949).

(115) Maschio, C., *Riv. Anat. Pat. 8,* 675-94 (1954).

(116) Matsuo, H., *Med. J. Osaka Univ. 5,* 763-76 (1954).

(117) Menkin, V., *Proc. A. A. Cancer Res. 2,* 34 (1955).

(118) Menkin, V., *ibid. 2,* 34 (1955).

(119) Millar, M. J. and Noble, R. L., *Brit. J. Cancer 8,* 495-507 (1954).

(120) Millar, M. J. and Noble, R. L., *ibid. 8,* 508-12 (1954).

(121) Miller, E. W. and Pybus, F. C., *ibid. 8,* 163-72 (1954).

(122) Miller, E. W. and Pybus, F. C., *ibid. 8,* 466-84 (1954).

(123) Miller, E. W. and Pybus, F. C., *ibid. 8,* 655-65 (1954).

(124) Miller, J. A., *et al., Proc. A. A. Cancer Res. 2,* 34-5 (1955).

(125) Miller, J. A., *et al., Cancer Res. 15,* 188-99 (1955).

(126) Miroff, G., *et al., ibid. 15,* 437-41 (1955).

(127) Moller, B., *Acta Path. Microbiol. 35,* 549-58 (1954).

(128) Moloney, W. C. and Kastenbaum, M. A., *Science 121,* 308-9 (1955).

(129) Muhlbock, O., *Acta Unio Intern. Contra Cancr. 10,* 140 (1954).

(130) Muhlbock, O., *ibid. 10,* 141-2 (1954).

(131) Mulay, A. S. and Congdon, C. C., *J. Natl. Cancer Inst. 14,* 571-83 (1953).

(132) Mulvany, D. K., *Lancet 2,* 205-6 (1953).

(133) Nagareda, C. S. and Kaplan, H. S., *Proc. A. A. Cancer Res. 2, 37* (1955).

(134) Newton, B. L., *ibid. 2,* 37-8 (1955).

(135) Norden, G. and Linell, F., *Acta Path. Microbiol. 35,* 433-6 (1954).

(136) Oppenheimer, B. S., *et al., Surg. Forum* 672-6 (1953).

(137) Oppenheimer, B. S., *et al., Cancer Res. 15,* 333-40 (1955).

(138) Pearson, B. and Defendi, V., *Proc. A. A. Cancer. Res. 2,* 39 (1955).

(139) Peller, S. and Pick, P., *Am. J. Med. Sci. 224,* 154-9 (1952).

(140) Pesonen, S., *Acta Endocrinol. 5,* 409-12 (1950).

(141) Pikovski, M. and Schlesinger, M., *Cancer Res. 15,* 285-90 (1955).

(142) Poel, W. E., *et al., Proc. A. A. Cancer Res. 2,* 40 (1955).

(143) Pybus, F. C. and Miller, E. W., *Ann. Rept. Brit. Emp. Cancer Campg. 30,* 205-11 (1952).

(144) Pyriki, C., Pharm. Zentralhalle *92*, 242-8 (1953).

(145) Rather, L. J., *Bull. Johns Hopkins Hosp. 88*, 38-58 (1951).

(146) Raynaud, A. and Raynaud, A., *Compt. Rend. Acad. Sci. 238*, 315-7 (1954).

(147) Richardson, H. L. and Pearson, B., *J. Natl. Cancer Inst. 14*, 1123-35 (1954).

(148) Richardson, H. L., *et al., Cancer 7*, 1044-7 (1954).

(149) Richardson, H. L., *Proc. A. A. Cancer Res. 2*, 41 (1955).

(150) Ritchie, A. C. and Saffiotti, U., *Cancer Res. 15*, 84-8 (1955).

(151) Roe, F. J. C. and Salaman, M. H., *Brit. J. Cancer 8*, 666-76 (1954).

(152) Rudali, G., *Compt. Rend. 146*, 1504-6 (1952).

(153) Rudali, G. and Royer, R., *ibid. 146*, 1531 (1952).

(154) Runner, M. N. and Dickie, M. M., *Proc. A. A. Cancer Res. 2*, 42-3 (1955).

(155) Saffiotti, N. and Shubik, P., *ibid. 2*, 43 (1955).

(156) Sampey, J. R., *J. So. Car. Med. Assoc. 51*, 316-8 (1955).

(157) Sampey, J. R., In press.

(158) Sapeika, N., *South African Med. J. 26*, 485-8 (1952).

(159) Schaeffer, A. E., *et al., J. Nutrition 43*, 201-21 (1951).

(160) Schinz, H. R. and Fritz-Niggli, H., *Strahlentherapie 94*, 554-60 (1954).

(161) Schneyer, C. A., *Cancer Res. 15*, 268-70 (1955).

(162) Schoental, R., *et al., Brit. J. Cancer 8*, 458-65 (1954).

(163) Scholler, J., *et al., Cancer Res. Suppl. 3*, 32-7 (1955).

(164) Schuren, Van G. and Debie, F., *Acta Unio Intern. Contra Cancr. 7*, 178-83 (1950).

(165) Seelkopf, C., *Z. Lehersm-Untersuch u. Forsch 100*, 218-22 (1955).

(166) Sherman, I. R., *et al., Abstracts ACS Meeting 112th*, 12 C (1953).

(167) Shubik, P. and Saffiotti, N., *Proc. A. A. Cancer Res. 2*, 46 (1955).

(168) Silberberg, R., *et al., Arch. Path. 53*, 506-15 (1953).

(169) Silberberg, R. and Silberberg, M., *Proc. A. A. Cancer Res. 2*, 46 (1955).

(170) Silberberg, M. and Silberberg, R., *Cancer Res. 15*, 291-3 (1955).

(171) Sissons, H. A., Acta Unio Intern. Contra *Cancr. 7*, 171-2 (1950).

(172) Snell, F. M., *et al., Arch. Int. Med. 84*, 569-604 (1949).

(173) Snell, G. D., *et al., Proc. A. A. Cancer Res. 2*, 47 (1955).

(174) Sobel, H. and Marmorston, J., *ibid. 2*, 47 (1955).

(175) Sokoloff, B., *ibid. 2*, 47 (1955).

(176) Stephenson, J. H. and Grace, W., J. *Psychosom. Med. 16*, 287-94 (1954).

(177) Stewart, H. L. and Hare, W. V., *Acta Unio Intern. Contra Cancr. 7*, 176-7 (1950).

(178) Stewart, S. E., *Proc. A. A. Cancer Res. 2,* 48 (1955).

(179) Strombeck, J. P. and Ekman, B., *Acta Path. Microbiol. 26,* 480-95 (1949).

(180) Teir, H., *et al., ibid. 93,* 93-7 (1952).

(181) Thiery, G., *Compt. Rend. 144,* 743-5 (1950).

(182) Thiery, G., *ibid. 144,* 745-7 (1950).

(183) Toch, P., *et al., Proc. A. A. Cancer Res. 2,* 51 (1955).

(184) Toolan, H. W., *ibid. 2,* 52 (1955).

(185) Toth, E., *et al., Acta Morph. 4,* 493-505 (1954).

(186) Truhaut, R., *Semaine Hop. 25,* 3078-84 (1949).

(187) Truhaut, R., *Arch. Ind. Hyg. 5,* 264-73 (1952).

(188) Tuba, J., *et al., Can. J. Med. Sci. 31,* 95-8 (1953).

(189) Vaggi, L., *Lav. Umano 7,* 111-32 (1949).

(190) Von Haam, E. and Scarpelli, D. G., *Cancer Res. 15,* 449-55 (1955).

(191) Walpole, A. L., *et al., Brit. J. Pharmacol. 9,* 306-23 (1954).

(192) Walpole, A. L., *et al., Acta Unio Intern. Contra Cancr. 10,* 174-5 (1954).

(193) Weston, J. T. and Guin, G. H., *Cancer 8,* 179-86 (1955).

(194) Wright, G. F. and Wynder, E. L., *Proc. A. A. Cancer Res. 2,* 55 (1955).

(195) Wynder, E. L., *et al., ibid. 2,* 56 (1955).

(196) Wynder, E. L., *et al., Cancer Res. 15,* 445-8 (1955).

(197) Zak, K., Lek. *Listy Brno 9,* 536-7 (1954).

(198) Zeitlhofer, J. and Speiser, P., *Z. Krebsforsch 60,* 161-8 (1954).

SELECTED ABSTRACTS

Dentrifices Evaluated in Dental Caries. Manly, R. S. *Drug & Cosm. Ind. 76:327* (1955). The evaluation of ingredients which show promise for use in dental preparations has been fraught with inconsistencies. Laboratory methods have frequently not correlated well with animal and clinical studies. A preliminary laboratory test is an essential tool for the dental research laboratory.

The author published the results of two laboratory tests employed with 11 compounds which had been tried in clinical experience. The saliva-glucose test has been used by a number of research workers but the salivary sediment test was developed by the author. The saliva glucose test involves incubation for about 4 hours of saliva from persons with active dental caries with from 2 to 10 per cent glucose and a variety of concentrations of the test compound. The pH, titratable acidity, or solution of calcium or phosphate from enamel or hydroxyapatite is determined. The end point is the concentration of the compound which just nullifies the effect of incubation with sugar.

The salivary sediment test involves the pooling and centrifuging of saliva from selected subjects. A known quantity of sediment is shaped over the active surface of a glass electrode with the aid of an open-mesh nylon thimble. The electrode and sediment are placed in a carbonate buffer containing glucose until the sediment pH becomes constant. At this point, the pH differential between the sediment and the solution is a measure of sediment activity. The sediment is then placed in a solution containing the test compound for 20 minutes. The sediment is removed, rinsed and returned to the control buffer until a steady state is again attained. The percentage reduction of the pH differential caused by the treatment indicates the degree of inhibition.

By the saliva-glucose test practically 100 per cent inhibition was recorded for ammonium phosphate, copper chlorophyllin, copper sulfate, sodium fluoride, glyceraldehyde, iodoacetate, N-lauroyl sarcosinate, penicillin, urea, and vitamin K. By the salivary sediment test, iodoacetate was about 80 per cent active, copper sulfate and N-lauroyl sarcosinate were about 60 per cent active, copper chlo-

rophyllin and penicillin were about 10 per cent active, and the others were inactive. Comparing these results with either animal or clinical tests it was found that the saliva-glucose test gave false positive test results in about 70 per cent of the studies. The salivary sediment test gave accurate correlation with either the animal or clinical tests.

The author concluded that the better performance of the sediment method could probably be attributed to its closer approximation of mouth conditions. The test substance must diffuse through a semisolid mass or organic substance that resembles the situation that must exist when a chemical in a dentifrice must affect dental plaques between teeth.

The Treatment of Rheumatoid Arthritis With Prednisone and Prednisolone. Hart, F. D., Clark, C. J., and Golding, J. R. *The Lancet 269:998* (1955). The effect of prednisone or prednisolone in 1/4 to 1/5 the dosage usually used with cortisone was compared with cortisone by changing from one to the other in 14 patients with rheumatoid arthritis. Pain and stiffness improved in 10 of the 14 cases when they were transferred from cortisone to prednisone. Likewise, joint tenderness improved in 10 cases and remained unchanged in 4 cases upon transferring from cortisone to prednisone. The power of grip was found to improve in 4 cases, remain unchanged in 8 and was not tested in 2. Walking time improved in 3, was unchanged in 7 and was not tested in 4. The effect on the erythrocyte sedimentation rate was 6, 8 and 0 and upon swelling of the proximal interphalangeal joints 8, 5 and 1, respectively. An over-all improvement was considered to have taken place in 10 cases while 4 others remained unchanged upon transferring from cortisone to prednisone or prednisolone.

Deterioration of the condition of the patients did not occur upon transfer from cortisone to prednisone or prednisolone. However, deterioration did occur in 8 patients upon transfer back to cortisone.

From this short-term study it would appear that prednisone or prednisolone are more effective in 1/4 to 1/5 the dosage than is cortisone in relieving the symptoms of rheumatoid arthritis. The period of treatment was from 4 days to 10 weeks. No toxic effects of the two new drugs were observed.

THE INDEX

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rophyllin and penicillin were about 10 per cent active, and the others were inactive. Comparing these results with either animal or clinical tests it was found that the saliva-glucose test gave false positive test results in about 70 per cent of the studies. The salivary sediment test gave accurate correlation with either the animal or clinical tests.

The author concluded that the better performance of the sediment method could probably be attributed to its closer approximation of mouth conditions. The test substance must diffuse through a semisolid mass or organic substance that resembles the situation that must exist when a chemical in a dentifrice must affect dental plaques between teeth.

The Treatment of Rheumatoid Arthritis With Prednisone and Prednisolone. Hart, F. D., Clark, C. J., and Golding, J. R. *The Lancet 269:998* (1955). The effect of prednisone or prednisolone in 1/4 to 1/5 the dosage usually used with cortisone was compared with cortisone by changing from one to the other in 14 patients with rheumatoid arthritis. Pain and stiffness improved in 10 of the 14 cases when they were transferred from cortisone to prednisone. Likewise, joint tenderness improved in 10 cases and remained unchanged in 4 cases upon transferring from cortisone to prednisone. The power of grip was found to improve in 4 cases, remain unchanged in 8 and was not tested in 2. Walking time improved in 3, was unchanged in 7 and was not tested in 4. The effect on the erythrocyte sedimentation rate was 6, 8 and 0 and upon swelling of the proximal interphalangeal joints 8, 5 and 1, respectively. An over-all improvement was considered to have taken place in 10 cases while 4 others remained unchanged upon transferring from cortisone to prednisone or prednisolone.

Deterioration of the condition of the patients did not occur upon transfer from cortisone to prednisone or prednisolone. However, deterioration did occur in 8 patients upon transfer back to cortisone.

From this short-term study it would appear that prednisone or prednisolone are more effective in 1/4 to 1/5 the dosage than is cortisone in relieving the symptoms of rheumatoid arthritis. The period of treatment was from 4 days to 10 weeks. No toxic effects of the two new drugs were observed.

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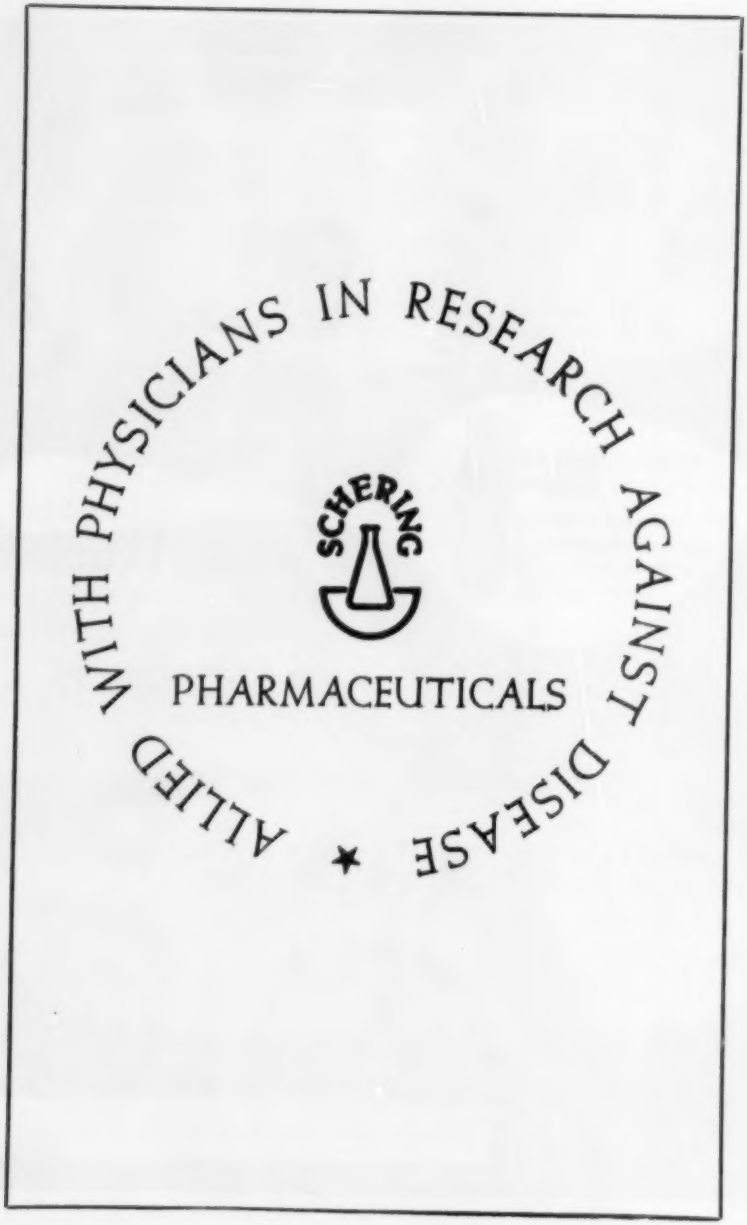
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